General

Guideline Title

Lung cancer. The diagnosis and treatment of lung cancer.

Bibliographic Source(s)

National Collaborating Centre for Cancer. Lung cancer. The diagnosis and treatment of lung cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. 42 p. (Clinical guideline; no. 121).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Acute Care. The diagnosis and treatment of lung cancer. London (UK): National Institute for Clinical Excellence (NICE); 2005 Feb. 350 p.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

New and updated recommendations are included on communication, diagnosis and staging, selection of patients with non-small-cell lung cancer (NSCLC) for treatment with curative intent, surgery with curative intent for NSCLC, smoking cessation, combination treatment for NSCLC, treatment for small-cell lung cancer (SCLC), managing endobronchial obstruction, managing brain metastases, and follow-up and patient perspectives. Recommendations are marked as [2005], [2011] or [new 2011]. [2005] indicates that the evidence has not been updated and reviewed since 2005. [2011] indicates that the evidence has been reviewed but no changes have been made to the recommendation. [new 2011] indicates that the evidence has been reviewed and the recommendation has been added or updated.

Note from NICE and NGC: The recommendations under "Referral and Indications for Chest Radiography" were replaced in July 2015 with updated guidance from NICE's "Suspected cancer: recognition and referral" guideline. The updated recommendations are labeled [new 2015].

Access to Services and Referral

The Importance of Early Diagnosis

The public needs to be better informed of the symptoms and signs that are characteristic of lung cancer, through coordinated campaigning to raise awareness. [2005]

Referral and Indications for Chest Radiography

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for lung cancer if they:

- Have chest X-ray findings that suggest lung cancer or
- Are aged 40 and over with unexplained haemoptysis. [new 2015]

Offer an urgent chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over if they have 2 or more of the following unexplained symptoms, or if they have ever smoked and have 1 or more of the following unexplained symptoms:

- Cough
- Fatigue
- Shortness of breath
- Chest pain
- Weight loss
- Appetite loss [new 2015]

Consider an urgent chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following:

- Persistent or recurrent chest infection
- Finger clubbing
- Supraclavicular lymphadenopathy or persistent cervical lymphadenopathy
- Chest signs consistent with lung cancer
- Thrombocytosis [new 2015]

Where a chest x-ray has been requested in primary or secondary care and is incidentally suggestive of lung cancer, a second copy of the radiologist's report should be sent to a designated member of the lung cancer MDT, usually the chest physician. The MDT should have a mechanism in place to follow up these reports to enable the patient's general practitioner to have a management plan in place. [2005]

Communication

Find out what the patient knows about their condition without assuming a level of knowledge. Provide patients with the opportunity to discuss tests and treatment options in a private environment, with the support of carers, and time to make an informed choice. [new 2011]

Ensure that a lung cancer clinical nurse specialist is available at all stages of care to support patients and carers. [new 2011]

Offer accurate and easy-to-understand information to patients and their carers. Explain the tests and treatment options, including potential survival benefits, side effects, and effect on symptoms. [new 2011]

Consider tailor-made decision aids to help patients to:

- Understand the probable outcomes of treatment options
- Consider the personal value they place on benefits versus harms of treatment options
- Feel supported in decision-making

- Move through the steps towards making a decision
- Take part in decisions about their healthcare. [new 2011]

Offer patients a record of all discussions that have taken place with them and a copy of any correspondence with other healthcare professionals. Ensure all communications are worded in such a way to assist understanding. [new 2011]

Respect the patient's choice if they do not wish to confront future issues. [new 2011]

Avoid giving patients unexpected bad news by letter. Only give unexpected bad news by phone in exceptional circumstances. [new 2011]

Offer to discuss end-of-life care with the patient sensitively and when appropriate. Wherever possible, avoid leaving this discussion until the terminal stages of the illness. [new 2011]

Document discussions with the patient about end-of-life care. In particular, document:

- Specific concerns of the patient
- Their understanding of their illness and its prognosis
- Important values or personal goals for care
- Their preferences for the types of care or treatment that may be beneficial in the future and their availability [new 2011]

Share information between healthcare professionals about:

- Any problems the patient has
- The management plan
- What the patient has been told
- What the patient has understood (where possible)
- The involvement of other agencies
- Any advance decision made by the patient [new 2011]

Diagnosis and Staging

Effectiveness of Diagnostic and Staging Investigations

Sputum cytology is rarely indicated and should be reserved for the investigation of patients who have centrally placed nodules or masses and are unable to tolerate, or unwilling to undergo, bronchoscopy or other invasive tests. [2005]

Patients with known or suspected lung cancer should be offered a contrast-enhanced chest computed tomography (CT) scan to further the diagnosis and stage the disease. The scan should also include the liver and adrenals*. [2005]

*This recommendation was outside the scope of the 2011 update but the guideline development group (GDG) recognised that many centres include the lower neck when performing CT scans for the diagnosis of lung cancer. The GDG also recognised that contrast medium should only be given with caution to patients with known renal impairment.

In the assessment of mediastinal and chest wall invasion:

- CT alone may not be reliable.
- Other techniques such as ultrasound should be considered where there is doubt.
- Surgical assessment may be necessary if there are no contraindications to resection. [2005]

Ensure all patients potentially suitable for treatment with curative intent are offered positron emission tomography-computed tomography (PET-CT) before treatment. [new 2011]

Every cancer network should have a system of rapid access to PET-CT scanning for eligible patients. [2005]

Magnetic resonance imaging (MRI) should not routinely be performed to assess the stage of the primary tumour (T-stage) in non-small-cell lung cancer (NSCLC). [2005]

MRI should be performed, where necessary to assess the extent of disease, for patients with superior sulcus tumours. [2005]

Offer endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) for biopsy of paratracheal and peri-bronchial intra-parenchymal lung lesions. [new 2011]

Every cancer network should have at least one centre with EBUS and/or endoscopic ultrasound (EUS) to ensure timely access. [new 2011]

The local test performance of non-ultrasound-guided TBNA, EBUS, and EUS-guided fine needle aspiration (FNA) should be the subject of audit. [new 2011]

Ensure adequate samples are taken without unacceptable risk to the patient to permit pathological diagnosis including tumour sub-typing and measurement of predictive markers. [new 2011]

Sequence of Investigations

Choose investigations that give the most information about diagnosis and staging with least risk to the patient. Think carefully before performing a test that gives only diagnostic pathology when information on staging is also needed to guide treatment. [new 2011]

Chest CT should be performed before:

- An intended fibreoptic bronchoscopy
- Any other biopsy procedure [2005]

Peripheral Primary Tumour

Offer CT- or ultrasound-guided transthoracic needle biopsy to patients with peripheral lung lesions when treatment can be planned on the basis of this test. [new 2011]

Biopsy any enlarged mediastinal nodes (≥10 mm maximum short axis on CT) or other lesions in preference to the primary lesion if determination of stage affects treatment*. [new 2011]

*Many patients with lung cancer will not be fit for treatment with curative intent. This needs to be taken into account when choosing diagnostic and staging investigations.

Central Primary Tumour

Offer fibreoptic bronchoscopy to patients with central lesions on CT where nodal staging does not influence treatment. Enlarged lymph nodes (≥10 mm maximum short axis on CT) may be simultaneously sampled with TBNA (non-ultrasound-guided) if required for diagnosis. [new 2011]

Mediastinal Lymph Node Assessment

Offer PET-CT as the preferred first test after CT showing a low probability of mediastinal malignancy (lymph nodes <10 mm maximum short axis on CT) for patients who are potentially suitable for treatment with curative intent. [new 2011]

Offer PET-CT, EBUS-guided TBNA, EUS-guided FNA, or non-ultrasound-guided TBNA as the first test for patients with an intermediate probability of mediastinal malignancy (lymph nodes between 10 and 20 mm maximum short axis on CT) who are potentially suitable for treatment with curative intent. [new 2011]

Offer neck ultrasound with sampling of visible lymph nodes or non-ultrasound-guided TBNA to patients with a high probability of mediastinal malignancy (lymph nodes >20 mm maximum short axis on CT). If neck ultrasound is negative, follow with non-ultrasound-guided TBNA, EBUS-guided TBNA, or EUS-guided FNA. If non-ultrasound-guided TBNA is negative follow with EBUS-guided TBNA or EUS-guided FNA. [new 2011]

Offer neck ultrasound with biopsy of visible lymph nodes to patients that have neck nodes detected by initial CT. If negative, follow with non-ultrasound-guided TBNA or EBUS-guided TBNA or EUS-guided FNA. [new 2011]

Evaluate PET-CT-positive mediastinal nodes by mediastinal sampling (except when there is definite distant metastatic disease or a high probability that N2/N3 disease is metastatic [for example, if there is a chain of lymph nodes with high ^{18}F-deoxyglucose uptake]). [new 2011]

Consider combined EBUS and EUS for initial staging of the mediastinum as an alternative to surgical staging. [new 2011]

Confirm negative results obtained by non-ultrasound-guided TBNA using EBUS-guided TBNA, EUS-guided FNA or surgical staging. [new 2011]

Confirm negative results obtained by EBUS-guided TBNA and/or EUS-guided FNA using surgical staging if clinical suspicion of mediastinal malignancy is high. [new 2011]

Stage M1b

Confirm the presence of isolated distant metastases/synchronous tumours by biopsy or further imaging (for example, MRI or PET-CT) in patients being considered for treatment with curative intent. [new 2011]

Consider MRI or CT of the head in patients selected for treatment with curative intent, especially in stage III disease. [new 2011]

Offer patients with features suggestive of intracranial pathology CT of the head followed by MRI if normal, or MRI as an initial test. [new 2011]

An x-ray should be performed in the first instance for patients with localised signs or symptoms of bone metastasis. If the results are negative or inconclusive, either a bone scan or an MRI scan should be offered. [2005]

Avoid bone scintigraphy when PET-CT has not shown bone metastases. [new 2011]

Organisational Factors Relevant to Diagnosis and Staging

Patients who have lung cancer suitable for radical treatment or chemotherapy, or need radiotherapy or ablative treatment for relief of symptoms, should be treated without undue delay, according to the Welsh Assembly Government and Department of Health recommendations (within 31 days of the decision to treat and within 62 days of their urgent referral). [2005]

Multidisciplinary Teams

All patients with a likely diagnosis of lung cancer should be referred to a member of a lung cancer MDT (usually a chest physician). [2005]

The care of all patients with a working diagnosis of lung cancer should be discussed at a lung cancer MDT meeting. [2005]

Rapid Access Lung Clinics

Rapid access clinics (previously known as early diagnosis clinics) should be provided where possible for the investigation of patients with suspected lung cancer, because they are associated with faster diagnosis and less patient anxiety. [2005]

Cancer Clinical Nurse Specialists

All cancer units/centres should have one or more trained lung cancer clinical nurse specialists to see patients before and after diagnosis, to provide continuing support, and to facilitate communication between the secondary care team (including the MDT), the patient's general practitioner, the community team and the patient. Their role includes helping patients to access advice and support whenever they need it. [2005]

Treatment

Smoking Cessation

Inform patients that smoking increases the risk of pulmonary complications after lung cancer surgery. [new 2011]

Advise patients to stop smoking as soon as the diagnosis of lung cancer is suspected and tell them why this is important. [new 2011]

Offer nicotine replacement therapy and other therapies to help patients to stop smoking in line with Smoking cessation services (NICE public health guidance 10) and Varenicline for smoking cessation (NICE technology appraisal guidance 123). [new 2011]

Do not postpone surgery for lung cancer to allow patients to stop smoking. [new 2011]

Selection of Patients with NSCLC for Treatment with Curative Intent

Perioperative Mortality

When evaluating surgery as an option for patients with NSCLC, consider using a global risk score such as Thoracoscore to estimate the risk of death. Ensure the patient is aware of the risk before giving consent for surgery. [new 2011]

Cardiovascular Function

Avoid surgery within 30 days of myocardial infarction. [new 2011]

Seek a cardiology review in patients with an active cardiac condition, or three or more risk factors, or poor cardiac functional capacity. [new 2011]

Offer surgery without further investigations to patients with two or fewer risk factors and good cardiac functional capacity. [new 2011]

Optimise any primary cardiac treatment and begin secondary prophylaxis for coronary disease as soon as possible. [new 2011]

Continue anti-ischaemic treatment in the perioperative period, including aspirin, statins, and beta-blockers. [new 2011]

If a patient has a coronary stent, discuss perioperative anti-platelet treatment with a cardiologist. [new 2011]

Consider revascularisation (percutaneous intervention or coronary artery bypass grafting) before surgery for patients with chronic stable angina and conventional indications for revascularisation. [new 2011]

Lung Function

Perform spirometry in all patients being considered for treatment with curative intent. Measure the transfer factor of the lung for carbon monoxide (T_LCO) if breathlessness is disproportionate or there is other lung pathology (for example, lung fibrosis). [new 2011]

Offer patients surgery if they have a forced expiratory volume in one second (FEV_1) within normal limits and good exercise tolerance. [new 2011]

Offer patients with predicted postoperative FEV_1 or T_LCO below the recommended limit of 30% the option of undergoing surgery if they accept the risks of dyspnoea and associated complications. [new 2011]

When considering surgery perform a segment count to predict postoperative lung function. [new 2011]

Consider using shuttle walk testing (using a distance walked of more than 400 m as a cut-off for good function) to assess fitness of patients with moderate to high risk of postoperative dyspnoea. [new 2011]

Consider cardiopulmonary exercise testing to measure maximum oxygen uptake (VO_2 max) and assess lung function in patients with moderate to high risk of postoperative dyspnoea, using more than 15 ml/kg/minute as a cut-off for good function. [new 2011]

Assessment before Radiotherapy with Curative Intent

A clinical oncologist specialising in thoracic oncology should determine suitability for radiotherapy with curative intent, taking into account performance status and comorbidities. [new 2011]

Surgery with Curative Intent for NSCLC

Offer patients with NSCLC who are medically fit and suitable for treatment with curative intent lobectomy (either open or thoracoscopic) as the treatment of first choice. For patients with borderline fitness and smaller tumours (T1a–b, N0, M0), consider lung parenchymal-sparing operations (segmentectomy or wedge resection) if a complete resection can be achieved. [new 2011]

Offer more extensive surgery (bronchoangioplastic surgery, bilobectomy, pneumonectomy) only when needed to obtain clear margins. [new 2011]

Perform hilar and mediastinal lymph node sampling or en bloc resection for all patients undergoing surgery with curative intent. [new 2011]

For patients with T3 NSCLC with chest wall involvement who are undergoing surgery, complete resection of the tumour should be the aim by either extrapleural or en bloc chest wall resection. [2005]

Radiotherapy with Curative Intent for NSCLC

Radical radiotherapy is indicated for patients with stage I, II, or III NSCLC who have good performance status (World Health Organization [WHO] 0, 1) and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage*. [2005]

*The GDG recognised that radiotherapy techniques have advanced considerably since the 2005 guideline and centres would reasonably wish to offer these techniques (including stereotactic body irradiation [SBRT] and four-dimensional [4-D] planning) to patients. These treatments have the advantage of reducing the risk of damage to normal tissue (estimated by using measurements such as the volume of lung that received at least 20 Grays (Gy) [V20]).

All patients should undergo pulmonary function tests (including lung volumes and transfer factor) before having radical radiotherapy for NSCLC. [2005]

Patients who have poor lung function but are otherwise suitable for radical radiotherapy should still be offered radiotherapy, provided the volume of irradiated lung is small. [2005]

Patients with stage I or II NSCLC who are medically inoperable but suitable for radical radiotherapy should be offered the continuous hyperfractionated accelerated radiotherapy (CHART) regimen. [2005]

Patients receiving radiotherapy with curative intent should be part of a national quality assurance programme*. [new 2011]

*The GDG recognised that radiotherapy techniques have advanced considerably since the 2005 guideline and centres would reasonably wish to offer these techniques (including SBRT and 4-D planning) to patients. These treatments have the advantage of reducing the risk of damage to normal tissue (estimated by using measurements such as V20).

Patients with stages IIIA or IIIB NSCLC who are eligible for radical radiotherapy and who cannot tolerate or do not wish to have chemoradiotherapy should be offered the CHART regimen. [2005]

If CHART is not available, conventionally fractionated radiotherapy to a dose of 64–66 Gy in 32–33 fractions over 6-1/2 weeks or 55 Gy in 20 fractions over 4 weeks should be offered. [2005]

Combination Treatment for NSCLC

Offer patients with stage I–III NSCLC who are not suitable for surgery an assessment by a clinical oncologist specialising in thoracic oncology for radiotherapy with curative intent. [new 2011]

Consider chemoradiotherapy for patients with stage II or III NSCLC who are not suitable for surgery. Balance potential benefit in survival with the risk of additional toxicities. [new 2011]

Ensure all patients potentially suitable for multimodality treatment (surgery, radiotherapy, and chemotherapy in any combination) are assessed by a thoracic oncologist and by a thoracic surgeon. [new 2011]

Offer postoperative chemotherapy to patients with good performance status (WHO 0 or 1) and T1–3, N1–2, M0 NSCLC. [new 2011]

Consider postoperative chemotherapy in patients with good performance status (WHO 0 or 1) and T2–3, N0, M0, NSCLC with tumours greater than 4 cm in diameter. [new 2011]

Offer a cisplatin-based combination chemotherapy regimen for adjuvant chemotherapy. [new 2011]

For patients with NSCLC who are suitable for surgery, do not offer neo-adjuvant chemotherapy outside a clinical trial. [new 2011]

Ensure eligible patients have the benefit of detailed discussion of the risks and benefits of adjuvant chemotherapy. [new 2011]

Treat Pancoast tumours in the same way as other types of NSCLC. Offer multimodality therapy according to resectability, stage of the tumour, and performance status of the patient. [new 2011]

Chemotherapy for NSCLC

Chemotherapy should be offered to patients with stage III or IV NSCLC and good performance status (WHO 0, 1 or a Karnofsky score of 80–100), to improve survival, disease control, and quality of life. [2005]

Chemotherapy for advanced NSCLC should be a combination of a single third-generation drug (docetaxel, gemcitabine, paclitaxel, or vinorelbine) plus a platinum drug. Either carboplatin or cisplatin may be administered, taking account of their toxicities, efficacy, and convenience. [2005]

Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy with a third-generation drug. [2005]

Docetaxel monotherapy should be considered if second-line treatment is appropriate for patients with locally advanced or metastatic NSCLC in whom relapse has occurred after previous chemotherapy. [2005]

Gefitinib

Refer to the NICE guideline Gefitinib for the First-line Treatment of Locally Advanced or Metastatic Non-small-cell Lung Cancer (NICE technology appraisal guidance 192 [2010]).

Pemetrexed

Refer to the NICE guideline Pemetrexed for the first-line Treatment of Non-small-cell Lung Cancer (NICE technology appraisal guidance 181 [2010]).

Erlotinib

See the NICE guideline Erlotinib for the treatment of non-small-cell lung cancer (NICE technology appraisal guidance 162 [2008]).

Assessing Patients with Small-Cell Lung Cancer

Arrange for patients with small-cell lung cancer (SCLC) to have an assessment by a thoracic oncologist within 1 week of deciding to recommend treatment. [new 2011]

First-Line Treatment for Limited-Stage Disease SCLC

Offer patients with limited-stage disease SCLC (broadly corresponding to T1–4, N0–3, M0) four to six cycles of cisplatin-based combination chemotherapy. Consider substituting carboplatin in patients with impaired renal function, poor performance status (WHO 2 or more), or significant comorbidity. [new 2011]

Offer concurrent chemoradiotherapy to patients with limited-stage disease SCLC (broadly corresponding to T1–4, N0–3, M0) and a WHO performance status of 0 or 1 if they present with disease that can be encompassed in a radical thoracic radiotherapy volume. Start the radiotherapy during the first or second cycle of chemotherapy. [new 2011]

Offer sequential radical thoracic radiotherapy to patients with limited-stage disease SCLC (broadly corresponding to T1–4, N0–3, M0) who are unfit for concurrent chemoradiotherapy but who respond to chemotherapy. [new 2011]

Surgical Treatment for Patients with SCLC

Consider surgery in patients with early-stage SCLC (T1–2a, N0, M0). [new 2011]

First-Line Treatment for Extensive-Stage Disease SCLC

Offer platinum-based combination chemotherapy to patients with extensive-stage disease SCLC (broadly corresponding to T1–4, N0–3, M1a/b – including cerebral metastases) if they are fit enough. [new 2011]

Assess the patient's condition before each cycle of chemotherapy for extensive-stage disease SCLC (broadly corresponding to T1–4, N0–3, M1a/b) and offer up to a maximum of six cycles, depending on response and toxicity. [new 2011]

For patients with extensive-stage disease SCLC, thoracic radiotherapy should be considered after chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax. [new 2011]

Maintenance Treatment for SCLC

Offer maintenance treatment to patients with SCLC only in the context of a clinical trial. [new 2011]

Prophylactic Cranial Irradiation in SCLC

Offer prophylactic cranial irradiation at a dose of 25 Gy in 10 fractions to patients with limited-stage disease SCLC and WHO performance status 2 or less, if their disease has not progressed on first-line treatment. [new 2011]

Offer prophylactic cranial irradiation to patients with extensive-stage disease SCLC and WHO performance status 2 or less, if their disease has not progressed on first-line treatment. [new 2011]

Second-Line Treatment for Patients with SCLC That has Relapsed after First-Line Treatment

Offer patients with SCLC that has relapsed after first-line treatment assessment by a thoracic oncologist. [new 2011]

Inform patients whose disease has not responded to first-line treatment that there is very limited evidence that second-line chemotherapy will be of benefit. [new 2011]

Offer patients with relapsed SCLC, who are suitable for chemotherapy, treatment with an anthracycline-containing regimen or further treatment with a platinum-based regimen to a maximum of six cycles. [new 2011]

Offer radiotherapy for palliation of local symptoms to patients with SCLC that has relapsed after first-line treatment. [new 2011]

Topotecan

Refer to the NICE guideline Topotecan for the Treatment of Small-cell lung cancer (NICE technology appraisal guidance 184 [2009]).

Palliative Interventions and Supportive and Palliative Care

Providing Palliative Care

Supportive and palliative care of the patient should be provided by general and specialist palliative care providers in accordance with the NICE guidance 'Improving supportive and palliative care for adults with cancer'. [2005]

Patients who may benefit from specialist palliative care services should be identified and referred without delay. [2005]

Palliative Radiotherapy

Patients who cannot be offered curative treatment, and are candidates for palliative radiotherapy, may either be observed until symptoms arise and then treated, or be treated with palliative radiotherapy immediately. [2005]

Managing Endobronchial Obstruction

When patients have large airway involvement, monitor (clinically and radiologically) for endobronchial obstruction to ensure treatment is offered early. [new 2011]

Offer external beam radiotherapy and/or endobronchial debulking or stenting to patients with impending endobronchial obstruction. [new 2011]

Every cancer network should ensure that patients have rapid access to a team capable of providing interventional endobronchial treatments. [new 2011]

Other Palliative Treatments

Pleural aspiration or drainage should be performed in an attempt to relieve the symptoms of a pleural effusion. [2005]

Patients who benefit symptomatically from aspiration or drainage of fluid should be offered talc pleurodesis for longer-term benefit. [2005]

Non-drug interventions based on psychosocial support, breathing control, and coping strategies should be considered for patients with breathlessness. [2005]

Non-drug interventions for breathlessness should be delivered by a multidisciplinary group, coordinated by a professional with an interest in breathlessness and expertise in the techniques (for example, a nurse, physiotherapist, or occupational therapist). Although this support may be provided in a breathlessness clinic, patients should have access to it in all care settings. [2005]

Opioids, such as codeine or morphine, should be considered to reduce cough. [2005]

Patients with troublesome hoarseness due to recurrent laryngeal nerve palsy should be referred to an ear, nose, and throat specialist for advice. [2005]

Patients who present with superior vena cava obstruction should be offered chemotherapy and radiotherapy according to the stage of disease and performance status. [2005]

Stent insertion should be considered for the immediate relief of severe symptoms of superior vena caval obstruction or following failure of earlier treatment. [2005]

Managing Brain Metastases

Offer dexamethasone to patients with symptomatic brain metastases and reduce to the minimum necessary maintenance dose for symptomatic response. [new 2011]

Consider palliative whole-brain radiotherapy for patients with symptomatic brain metastases with good performance status (WHO 0 or 1). [new 2011]

Hypercalcaemia, Bone Pain, and Pathological Fractures

For patients with bone metastasis requiring palliation and for whom standard analgesic treatments are inadequate, single-fraction radiotherapy should be administered. [2005]

Managing Other Symptoms: Weight Loss, Loss of Appetite, Difficulty Swallowing, Fatigue, and Depression

Other symptoms, including weight loss, loss of appetite, depression, and difficulty swallowing, should be managed by multidisciplinary groups that include supportive and palliative care professionals. [2005]

Follow-Up and Patient Perspectives

Offer all patients an initial specialist follow-up appointment within 6 weeks of completing treatment to discuss ongoing care. Offer regular appointments thereafter, rather than relying on patients requesting appointments when they experience symptoms. [new 2011]

Offer protocol-driven follow-up led by a lung cancer clinical nurse specialist as an option for patients with a life expectancy of more than 3 months. [new 2011]

Ensure that patients know how to contact the lung cancer clinical nurse specialist involved in their care between their scheduled hospital visits. [new 2011]

The opinions and experiences of lung cancer patients and carers should be collected and used to improve the delivery of lung cancer services. Patients should receive feedback on any action taken as a result of such surveys. [2005]

Clinical Algorithm(s)

The following clinical algorithms are provided in the full version of the original guideline document:

- Diagnostic and Staging Clinical Pathway
- Detail of Mediastinal Diagnosis and Staging
- Fitness Assessment Clinical Pathway

Scope

Disease/Condition(s)

Lung cancer (including small cell lung cancer and non-small cell lung cancer)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nuclear Medicine

Nursing

Oncology

Pathology

Psychology

Pulmonary Medicine

Radiation Oncology

Radiology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Hospitals

Nurses

Occupational Therapists

Patients

Pharmacists

Physical Therapists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Respiratory Care Practitioners

Social Workers

Guideline Objective(s)

- To provide recommendations for good practice in the diagnosis and treatment of non-small-cell (NSCLC) and small-cell lung cancer (SCLC)
- To offer best practice advice on the care of adults with lung cancer

Target Population

Adults (18 years and older) with newly diagnosed non-small cell lung cancer (NSCLC), newly diagnosed small cell lung cancer (SCLC), relapsed NSCLC, and relapsed SCLC

Note: These guidelines are not intended for use in the following populations:

Adults with mesothelioma
Adults with lung metastases arising from primary cancers originating outside the lung

Children (younger than 18) with lung cancer
Adults with rare lung tumours (for example, pulmonary blastoma)
Adults with benign lung tumours (for example, bronchial adenoma)

Interventions and Practices Considered

General

1. Providing information and support to patients
2. Effective communication with patients
3. Effective communication among the multidisciplinary team (MDT)

Diagnosis and Staging

1. Urgent chest x-ray for patients presenting with haemoptysis or other key symptoms/signs
2. Urgent referral to lung cancer MDT
3. Sputum cytology (not routinely recommended)
4. Contrast-enhanced computed tomography (CT) (including chest, liver, adrenals, lower neck)
5. Positron-emission tomography-computed tomography (PET-CT) scanning
6. Magnetic resonance imaging (MRI)
7. Endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA)
8. Endoscopic ultrasound (EUS)-guided fine-needle aspiration (FNA)
9. Non-ultrasound-guided TBNA
10. Biopsy of enlarged mediastinal nodes
11. Fibreoptic bronchoscopy
12. MRI and CT of head for suspected intracranial pathology
13. X-ray of localized bone metastases

Treatment/Management

1. Assessing fitness for treatment
2. Smoking cessation advice and treatment
3. Surgery with curative intent for non-small-cell lung cancer (NSCLC)
4. Radiotherapy with curative intent for NSCLC (continuous hyperfractionated accelerated radiotherapy [CHART] or conventional fractionated radiotherapy)
5. Combination modality therapy for NSCLC
6. Chemotherapy for NSCLC
    - Single third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine) plus a platinum drug (either carboplatin or cisplatin)
    - Single-agent chemotherapy with a third-generation drug
    - Docetaxel monotherapy for second-line treatment
    - Gefitinib, pemetrexed or erlotinib
7. Treatment of small-cell lung cancer
    - Surgery
    - Platinum-based combination therapy
    - Concurrent or sequential radiotherapy
    - Prophylactic cranial irradiation
    - Second-line chemotherapy (anthracycline-containing regimen or further platinum)
    - Second-line radiation therapy
    - Topotecan
8. Palliative care
    - Palliative radiation therapy
    - Managing endobronchial obstruction
    - Managing pleural effusion, breathlessness, cough, hoarseness, and other symptoms
    - Managing superior vena cava obstruction
    - Managing brain and bone metastases

9. Follow-up

Major Outcomes Considered

- Use and acceptability of patient decision aids
- Effectiveness, accuracy, sensitivity, and specificity of diagnostic tests
- Effectiveness of treatments
- Morbidity and mortality
- Survival
- Complications after surgery
- Rates of cancer recurrence and metastasis
- Detection of cancer recurrence
- Effectiveness of palliative treatments
- Quality of life
- Cost-effectiveness
- Quality adjusted life years

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing Clinical Evidence-based Questions

Background

The list of key clinical issues listed in the scope (see the "Description of Methods Used to Formulate the Recommendations" field) were developed in areas that were known to be controversial or uncertain, where there was identifiable practice variation, or where NICE guidelines were likely to have most impact.

Method

From each of the key clinical issues identified in the scope the Guideline Development Group (GDG) formulated a clinical question. For clinical questions about interventions, the patient, information, comparison, outcome (PICO) framework was used. This structured approach divides each question into four components: the population (the population under study – P), the interventions (what is being done – I), the comparisons (other main treatment options – C), and the outcomes (the measures of how effective the interventions have been – O). Where appropriate, the clinical questions were refined once the evidence had been searched and, where necessary, sub-questions were generated. The final list of clinical questions can be found in Appendix 8 of the full version of the original guideline document.

Review of Clinical Literature

Scoping Search

An initial scoping search for published guidelines, systematic reviews, economic evaluations, and ongoing research was carried out on the following databases or websites: National Library for Health (NLH) Guidelines Finder (now National Health Service [NHS] Evidence), National Guideline Clearinghouse, Cochrane Database of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA), NHS Economic Evaluations Database (NHSEED), DH Data, Medline, and EMBASE.

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national, or international) produced by other groups or institutions.

Searching for the Evidence

In order to answer each question the National Collaborating Centre for Cancer (NCC-C) information specialist developed a search strategy to identify relevant published evidence for both clinical and cost effectiveness. Key words and terms for the search were agreed in collaboration with the GDG. When required, the health economist searched for supplementary papers to inform detailed health economic work (see section on 'Incorporating Health Economic Evidence').

For those clinical topics that were updated from the 2005 guideline, searches were set to only identify evidence published after December 2003 to ensure no relevant papers were missed. No date limits were applied to searches carried OUT on new topics within the 2011 guideline.

Papers that were published or accepted for publication in peer-reviewed journals were considered as evidence. Search filters, such as those to identify systematic reviews and randomised controlled trials (RCTs) were applied to the search strategies when there was a wealth of these types of studies. No language restrictions were applied to the search; however, foreign language papers were not requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1950 onwards
- Excerpta Medica (EMBASE) 1980 onwards
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) 1982 onwards
- Allied & Complementary Medicine (AMED) 1985 onwards
- British Nursing Index (BNI) 1985 onwards
- PsycINFO 1806 onwards
- Web of Science (specifically Science Citation Index Expanded [SCI-EXPANDED] 1899 onwards and Social Sciences Citation Index (SSCI) 1956 onwards
- Biomed Central 1997 onwards

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

Searches were updated and re-run 6–8 weeks before the stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, 1st August 2010 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review (Appendix 11 to the full version of the guideline; see the "Availability of Companion Documents" field).

Critical Appraisal

From the literature search results database, a researcher scanned the titles and abstracts of every article for each question and full publications were ordered for any studies considered relevant or if there was insufficient information from the title and abstract to inform a decision. When the papers were obtained the researcher applied inclusion/exclusion criteria to select appropriate studies which were then critically appraised.

Literature searches were repeated for all of the clinical questions at the end of the GDG development process, allowing any relevant papers published before 1 August 2010 to be considered. Future guideline updates will consider evidence published after this cut-off date.

Incorporating Health Economic Evidence

In order to assess the cost-effectiveness of each priority topic, a broad review of the economic literature was conducted. The search strategy was designed to find any applied study estimating the cost or cost-effectiveness of any topic relating to lung cancer. A health economist reviewed abstracts and relevant papers were ordered for appraisal. Where it was judged that an economic question could be answered by a review of existing literature alone this was presented alongside the review of the clinical evidence. Otherwise, relevant papers were used to inform the design of the independent modelling. Studies that were not likely to provide useful information for guideline decision-making were not critically appraised.

Published economic evidence was obtained from a variety of sources:

- Medline 1966 onwards
- EMBASE 1980 onwards
- NHSEED
- EconLit 1969 onwards

For the clinical questions where an economic model was required, the information specialist performed supplemental literature searches to obtain additional data for modelling.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Critical Appraisal

For each question, data on the type of population, intervention, comparator and outcomes (PICO) were extracted and recorded in evidence tables and an accompanying evidence summary prepared (including meta-analyses where appropriate) for the Guideline Development Group (GDG) (see evidence review [Appendix 11 to the full version of the guideline; see the "Availability of Companion Documents" field]). All evidence was considered carefully by the GDG for accuracy and completeness.

All procedures were fully compliant with National Institute of Health and Clinical Effectiveness (NICE) methodology as detailed in the guidelines manual (NICE 2007; see the "Availability of Companion Documents" field). In general, no formal contact was made with authors; however, there were ad hoc occasions when this was required in order to clarify specific details.

Incorporating Health Economic Evidence

Economic Modelling

In addition to the review of the relevant clinical evidence, the GDG were required to determine whether or not the cost-effectiveness of each of the individual clinical questions should be investigated. After the clinical questions were decided, the GDG agreed which topics were priorities for economic modelling. These 'economic priorities' were chosen on the basis of the following criteria, in accordance with the guidelines manual.

Overall Relevance of the Topic

- *The number of patients affected*: Interventions affecting relatively large numbers of patients were given a higher economic priority than those affecting fewer patients.

- *The health benefits to the patient*: Interventions that were considered to have a potentially significant impact on both survival and quality of life were given a higher economic priority.
- *The per patient cost*: Interventions with potentially high financial (cost/savings) implications were given high priority compared to interventions expected to have lower financial implications.
- *Likelihood of changing clinical practice*: Priority was given to topics that were considered likely to represent a significant change to existing clinical practice.

Uncertainty

- *High level of existing uncertainty*: Higher economic priority was given to clinical questions in which further economic analysis was considered likely to reduce current uncertainty over cost-effectiveness. Low priority was given to clinical questions when the current literature implied a clearly 'attractive' or 'unattractive' incremental cost-effectiveness ratio, which was regarded as generalisable to a UK healthcare setting.
- *Likelihood of reducing uncertainty with further analyses (feasibility issues)*: When there was poor evidence for the clinical effectiveness of an intervention, then there was considered to be less justification for an economic analysis to be undertaken.

Once the economic priority clinical questions had been chosen, a feasibility assessment was carried out to determine the potential value of conducting independent modelling for each economic priority topic. This assessment was written up in the 'Economic Plan' (see full evidence review [Appendix 11 to the full version of the guideline; see the "Availability of Companion Documents" field]). After careful consideration by the GDG it was decided that a full economic analysis would only be carried out for one clinical question. The decision was based on the size and scale of the topic and the time and resource available to the health economist and the NCC-C.

For the clinical questions where an economic model was required, the information specialist performed supplemental literature searches to obtain additional data for modelling. Assumptions and designs of the models were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

The clinical question in this guideline selected for modelling was chosen because at the time it was considered likely that the recommendations under consideration could substantially change clinical practice in the National Health Service (NHS) and have important consequences for resource use. The details of the model are presented in the evidence review (Appendix 11 to the full version of the guideline; see the "Availability of Companion Documents" field) and Appendix 4 of the full version of the original guideline document.

During the modelling process the following general principles were adhered to:

- The GDG Chair, Clinical Lead, and other members of the GDG that formed the topic subgroup were consulted during the construction and interpretation of the model.
- The model assumptions were plausible and were reported fully and transparently.
- The model was based on the best available evidence from relevant systematic reviews or national audit data.
- The costs were calculated from a health services perspective.
- The results were discussed and tested using sensitivity analysis.
- The limitations of the model were acknowledged and discussed.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The Guideline Development Group (GDG)

The lung cancer GDG was recruited in line with the existing NICE protocol as set out in the 'guidelines manual' (NICE 2007). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and candidates were interviewed prior to being offered the role.

The NCC-C Director, GDG Chair and Lead Clinician identified a list of specialties that needed to be represented on the GDG. Requests for applications were sent to the main stakeholder organisations, cancer networks and patient organisations/charities (see Appendix 9.2 of the full version of the original guideline). Individual GDG members were selected by the NCC-C Director, GDG Chair and Lead Clinician, based on their application forms. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economic literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to drafting the guideline.

Guideline Development Group Meetings

Eleven GDG meetings were held between 12 February 2009 and 24 June 2010. During each GDG meeting (either held over one or two days) clinical questions and clinical and economic evidence were reviewed, assessed, and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed as part of a standing agenda item.

NCC-C project managers divided the GDG workload by allocating specific clinical questions, relevant to their area of clinical practice, to small subgroups of the GDG in order to simplify and speed up the guideline development process. These groups considered the evidence, as reviewed by the researcher, and synthesised it into draft recommendations prior to presenting it to the GDG as a whole. Each clinical question was led by a GDG member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GDG subgroups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Members

Individuals with direct experience of lung cancer gave an integral user focus to the GDG and the guideline development process. The GDG included three patient/carer members. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline, and bringing service-user research to the attention of the GDG.

Needs Assessment

As part of the guideline development process the NCC-C invited a specialist registrar, with the support of the GDG, to undertake a needs assessment (see Appendix 9.3 of the full version of the original guideline document). The needs assessment aims to describe the burden of disease and current service provision for patients with lung cancer in England and Wales, which informed the development of the guideline.

Assessment of the effectiveness of interventions is not included in the needs assessment, and was undertaken separately by researchers in the NCC-C as part of the guideline development process.

The information included in the needs assessment document was presented to the GDG. Most of the information was presented in the early stages of guideline development, and other information was included to meet the evolving information needs of the GDG during the course of guideline development.

The Scope

The scope was prepared by the GDG Chair and Lead Clinician and staff at the NCC-C in accordance with processes established in the guidelines manual (NICE 2007). The recommendations of the expert advisory group were carefully considered and subsequently included in the scope where appropriate. The purpose of the scope was to:

- Set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC-C and the remit set by the Department of Health
- Inform professionals and the public about the expected content of the guideline
- Provide an overview of the population and healthcare settings the guideline would include and exclude
- Specify the key clinical issues that will be covered by the guideline
- Inform the development of the clinical questions and search strategy

The scope was subject to a four week stakeholder consultation in accordance with processes established by NICE in the 'guidelines manual' (NICE 2007). The full scope is shown in Appendix 7. During the consultation period, the scope was posted on the NICE website (www.nice.org.uk). Comments were invited from registered stakeholder organisations and the NICE Guideline Review Panel (GRP). Further information about the GRP can also be found on the NICE website. The NCC-C and NICE reviewed the scope in light of comments received, and the revised scope was reviewed by the GRP, signed off by NICE and posted on the NICE website.

Agreeing the Recommendations

For each clinical question the GDG were presented with a summary of the clinical evidence, and where appropriate economic evidence, derived from the studies reviewed and appraised. From this information the GDG were able to derive the guideline recommendations. The link between the evidence and the view of the GDG in making each recommendation is made explicit in the accompanying qualifying statement.

Qualifying Statements

As clinical guidelines are currently formatted, there is limited scope for expressing how and why a GDG made a particular recommendation from the evidence of clinical and cost-effectiveness. To make this process more transparent to the reader, the NCC-C felt the need for an explicit, easily understood, and consistent way of expressing the reasons for making each recommendation.

The way the guideline authors have chosen to do this is by writing a 'qualifying statement' to accompany every recommendation and usually covering:

- The strength of evidence about benefits and harms for the intervention being considered
- The degree of consensus within the GDG
- The costs and cost-effectiveness of an intervention (if formally assessed by the health economics team)

Where evidence was weak or lacking the GDG agreed the final recommendations through informal consensus. Shortly before the consultation period, ten key priorities and five key research recommendations were selected by the GDG for implementation and the patient algorithms were agreed. To avoid giving the impression that higher grade recommendations are of higher priority for implementation, NICE no longer assigns grades to recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Economic Model to Compare Different Testing Strategies to Stage the Mediastinum in Patients with Non-Small-Cell Lung Cancer

The aim of this analysis was to assess the cost utility of clinically relevant alternative sequences of tests to stage the mediastinum in three subgroups of patients with non-small-cell lung cancer (NSCLC) from a UK National Health Services (NHS) perspective. See table A4.1 in the full version of the original guideline document.

The results of the cost-effectiveness analyses show that different sequences of staging tests are likely to be cost-effective in different subgroups of patients. The results show that in the low cancer prevalence population there are only small differences in quality-adjusted life years (QALYs) between strategies involving positron emission tomography-computed tomography (PET-CT), roughly equivalent to just over 16 days in full health. However, when this is put in context of lung cancer, where utility values are likely to be much lower than perfect health, this difference is not inconsiderable. The results in the low prevalence group show that PET-CT on its own is clearly the most cost-effective alternative (of the strategies considered) and seems robust to deterministic sensitivity analysis of several parameters. The results of the analysis in the intermediate cancer prevalence subgroup showed more variation in overall expected costs and health benefits. The incremental analysis revealed that strategy 2, PET-CT followed by transbronchial needle aspiration (TBNA) at an incremental cost-effectiveness ratio of £19,448 per QALY. However, due to the multitude of strategies in the analysis, these results of the analysis in this subgroup need careful interpretation. Since there is little difference in terms of QALYs between several strategies (particularly between strategies 3 [PET-CT followed by endobronchial ultrasound (EBUS)], 4 [PET-CT followed by TBNA and EBUS], 6 [PET-CT followed by EBUS and mediastinoscopy (Med)], 14 [Neck ultrasound (US) followed by EBUS and PET-CT], and 22 [Neck US followed by TBNA, EBUS, and PET-CT]) and given the uncertainty surrounding these point estimates, there is likely to be some ambiguity over which strategy dominates, and thus which should be excluded from the incremental analysis.

The results in the high cancer prevalence population showed that strategy 13 (Neck US followed by TBNA and PET-CT) is both cheapest and most clinically effective and therefore most cost-effective, dominating all other clinically relevant strategies for that subgroup. The results are summarised in Table A4.16 in the full version of the original guideline document.

These results may seem on the surface to be counter-intuitive. Those sequences of tests which lead to more accurate staging information do not lead to overall better outcomes for patients. However, test performance is only a surrogate endpoint – and the results of all three analyses are heavily dependent on assumptions made about downstream treatment decisions. Within the context of the model, strategies resulting in a higher number of false negatives allow a great proportion of patients with N2/3 disease to be offered surgery and other treatment with curative intent

options. Similarly if metastatic disease is missed, patients still achieve better outcomes with (inappropriate?) treatment with curative intent than with no anti-cancer treatment. These assumptions have been discussed in depth with the GDG, but it was decided that they hold and thus the results of the model logically follow from these assumptions.

There are a number of limitations to the analysis. In dichotomising the test results the analysts may have omitted several important factors. The possibility of a non-diagnostic test is not considered in the model which may bias the results towards EBUS and against mediastinoscopy. In fact they only considered the impact of tests on staging mediastinal disease for resectability, which limits the usefulness of tests like PET-CT. They also made some strong assumptions in order to evaluate test sequences which have not been analysed in the context of randomised controlled trials. For example they assumed if a test is positive, no confirmatory tests are required and additionally that the choice of treatment is solely determined by the result of the final test.

The analysts were not able to model the choice between EBUS and EUS (FNA), which they know in reality are used as complementary tools in assessing stage of disease. In the circumstance where either test is considered appropriate, they would need data on the location of nodes sampled using these tests and test accuracy for each test in order to model the choice between them.

Additionally, despite the wealth of data on test accuracy, the analysts were unable to pool it and use it to populate the model, as the data were not reported in terms of the three different subgroups of interest and instead had to rely on expert opinion.

The survival estimates used in the model were estimates of achieved survival of patients recorded in the National Lung Cancer Audit (NLCA). This obviously increases the generalisability of the model results since many lung cancer patients are treated in the NHS that would not be eligible for a randomised clinical trial, however the results might be different if the analysts used data from randomised controlled trials (RCTs) to populate the model with achievable survival for each treatment. Additionally, a strong assumption was made in fitting a Weibull distribution to the data. Given time and resource constraints, it was not possible to investigate the impact different distributions might have had the model results.

The analysts accounted for co-morbidities present in real-life patients by using the proportions of patients receiving treatment as recorded in NLCA, which show a high proportion of all patients not receiving treatment with curative intent in all stages of disease. However they did not investigate different sequences of staging tests for patients who could be identified as having co-morbidities upfront.

The sensitivity analysis performed showed the model was reasonably robust to changes in the treatment options, the choice of radiotherapy schedules, the price of chemotherapy drugs, the price of diagnostic tests, the death rate from mediastinoscopy, changes in utility values, as well as some assumptions about the choice of survival estimates for patients incorrectly staged.

Other assumptions about utility values could not be tested without changing the model structure. Test accuracy data was not available for the three subgroups identified as relevant to the decision problem; as such the analysts have relied on the expert opinion of the GDG. Ideally they would have wanted to conduct a probabilistic sensitivity analysis and a value of information analysis to quantify the maximum value of conducting research in this area.

The choice of clinically relevant sequences of tests considered in each subgroup analysis was not tested, and due to the incremental nature of the analysis will certainly influence the model results.

Despite these acknowledged limitations, these three analyses provided the GDG with useful information used in its deliberations over the recommendations to be made on this topic, particularly in the absence of any evidence from the UK of clinical as well as cost-effectiveness on the best sequence in which to use tests to stage mediastinal disease, in different subgroups of patients.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Consultation and Validation of the Guideline

The draft of the guideline was prepared by National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Development Group (GDG) Chair and Lead Clinician. This was then discussed and agreed with the GDG and subsequently forwarded to the National Institute for Health and Clinical Excellence (NICE) for consultation with stakeholders.

Registered stakeholders (see Appendix 9.2 of the full version of the original guideline document) had one opportunity to comment on the draft guideline which was posted on the NICE website between 4 October 2010 and 29 November 2010 in line with NICE methodology. The Guideline Review Panel (GRP) also reviewed the guideline and checked that stakeholder comments had been addressed.

The Pre-publication Check Process

Following stakeholder consultation and subsequent revision, the draft guideline was then subject to a pre-publication check. The pre-publication check provides registered stakeholders with the opportunity to raise any concerns about factual errors and inaccuracies that may exist in the revised guideline after consultation.

During the pre-publication check the full guideline was posted on the NICE website for 15 working days, together with the guideline consultation table that listed comments received during consultation from stakeholders and responses from the NCC-C and GDG.

All stakeholders were invited to report factual errors using a standard proforma. NICE, the NCC and the GDG Chair and Lead Clinician considered the reported errors and responded only to those related to factual errors. A list of all corrected errors and the revised guideline were submitted to NICE, and the revised guideline was then signed off by Guidance Executive. The list of reported errors from the pre-publication check and the responses from the NCC-C were subsequently published on the NICE website.

The final document was then submitted to NICE for publication on their website. The other versions of the guideline (see the "Availability of Companion Documents" field) were also discussed and approved by the GDG and published at the same time.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of the diagnosis and treatment of lung cancer, which may result in decreased morbidity and mortality

Potential Harms

- Complications of invasive diagnostic procedures
- Side effects and toxicities of treatment

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with

compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the NICE Web site (http://guidance.nice.org.uk/CG121 ; see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

The Importance of Early Diagnosis

- The public needs to be better informed of the symptoms and signs that are characteristic of lung cancer, through coordinated campaigning to raise awareness. [2005]

Communication

- Ensure that a lung cancer clinical nurse specialist is available at all stages of care to support patients and carers. [new 2011]

Diagnosis and Staging

- Choose investigations that give the most information about diagnosis and staging with the least risk to the patient. Think carefully before performing a test that gives only diagnostic pathology when information on staging is also needed to guide treatment. [new 2011]
- Offer positron emission tomography-computed tomography (PET-CT), or endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA), or endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA), or non-ultrasound-guided TBNA as the first test for patients with an intermediate probability of mediastinal malignancy (lymph nodes between 10 and 20 mm maximum short axis on computed tomography [CT]) who are potentially suitable for treatment with curative intent. [new 2011]

Surgery with Curative Intent for Non-Small Cell Lung Cancer

- Offer patients with non-small cell lung cancer (NSCLC) who are medically fit and suitable for treatment with curative intent lobectomy (either open or thoracoscopic) as the treatment of first choice. For patients with borderline fitness and smaller tumours (T1a–b, N0, M0), consider lung parenchymal-sparing operations (segmentectomy or wedge resection) if a complete resection can be achieved. [new 2011]

Radiotherapy with Curative Intent for NSCLC

- Radical radiotherapy is indicated for patients with stage I, II, or III NSCLC who have good performance status (World Health Organisation [WHO] 0, 1) and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage*. [2005]

*The Guideline Development Group recognised that radiotherapy techniques have advanced considerably since the 2005 guideline and centres would reasonably wish to offer these techniques (including stereotactic body radiation therapy [SBRT] and four-dimensional [4-D] planning) to patients. These treatments have the advantage of reducing the risk of damage to normal tissue (estimated by using measurements such as the volume of lung receiving at least 20 Grays [V20]).

Combination Treatment for NSCLC

- Ensure all patients potentially suitable for multimodality treatment (surgery, radiotherapy, and chemotherapy in any combination) are assessed by a thoracic oncologist and by a thoracic surgeon. [new 2011]

Assessing Patients with Small-Cell Lung Cancer

- Arrange for patients with small-cell lung cancer (SCLC) to have an assessment by a thoracic oncologist within 1 week of deciding to recommend treatment. [new 2011]

Managing Endobronchial Obstruction

- Every cancer network should ensure that patients have rapid access to a team capable of providing interventional endobronchial treatments. [new 2011]

Follow-up and Patient Perspectives

- Offer all patients an initial specialist follow-up appointment within 6 weeks of completing treatment to discuss ongoing care. Offer regular appointments thereafter, rather than relying on patients requesting appointments when they experience symptoms. [new 2011]

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Cancer. Lung cancer. The diagnosis and treatment of lung cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. 42 p. (Clinical guideline; no. 121).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2005 Feb (revised 2011 Apr)

Guideline Developer(s)

National Collaborating Centre for Cancer - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

Guideline Development Group Members: Mr Barrie White, Neurosurgeon, Queens Medical Centre, Nottingham; Professor Mark Baker, Divisional Medical Director for Oncology and Surgery and Lead Cancer Clinician, Leeds Teaching Hospitals NHS Trust; Dr David Baldwin, Consultant Physician, Nottingham University Hospital NHS Trust; Barry Attwood, Patient and carer member; Mr Sion Barnard, Consultant Thoracic Surgeon, Freeman Hospital, Newcastle-upon-Tyne; Dr Jeremy Braybrooke, Consultant Medical Oncologist, University Hospitals Bristol NHS Foundation Trust; Dr Paul Cane, Consultant Histopathologist, Guys & St Thomas' NHS Foundation Trust, London; Dr James Entwisle, Consultant Radiologist, Glenfield Hospital, University Hospitals of Leicester NHS Trust; Dr Jesme Fox, Patient and carer member, The Roy Castle Lung Cancer Foundation; Thomas Haswell, Patient and carer member; Mr Matthew Hatton, Consultant Clinical Oncologist, Weston Park Hospital, Sheffield; Dana Knoyle, Macmillan Lung Cancer Nurse Specialist, Prince Charles Hospital, Cwm Taf Health Board; Dr Richard Neal, Senior Lecturer in General Practice, North Wales Clinical School, Cardiff University; Mr Richard Page, Consultant Thoracic Surgeon, Liverpool Heart and Chest Hospital; Bob Park, Director, North East London Cancer Network; Sue Pascoe, Lung Cancer Clinical Nurse Specialist, Royal Cornwall Hospital; Dr Michael Peake, Consultant and Senior Lecturer in Respiratory Medicine, Glenfield Hospital, University Hospitals of Leicester NHS Trust; Dr Robert Rintoul, Consultant Respiratory Physician, Papworth Hospital NHS Foundation Trust, Cambridge; Dr Andrew Wilcock, Macmillan Clinical Reader in Palliative Medicine and Medical Oncology, University of Nottingham

Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix 9.1 of the full version of the original guideline document).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Acute Care. The diagnosis and treatment of lung cancer. London (UK): National Institute for Clinical Excellence (NICE); 2005 Feb. 350 p.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Lung cancer. The diagnosis and treatment of lung cancer. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. 198 p. (Clinical guideline; no. 121). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .
- Lung cancer. The diagnosis and treatment of lung cancer. Appendices to full version. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. (Clinical guideline; no. 121). Electronic copies: Available in PDF from the NICE Web site .
- Lung cancer. The diagnosis and treatment of lung cancer. Clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. (Clinical guideline; no. 121). Electronic copies: Available from the NICE Web site .
- Lung cancer. The diagnosis and treatment of lung cancer (update). Costing report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. 28 p. (Clinical guideline; no. 121). Electronic copies: Available in PDF from the NICE Web site .
- Lung cancer. The diagnosis and treatment of lung cancer. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. (Clinical guideline; no. 121). Electronic copies: Available from the NICE Web site .
- Lung cancer. Implementing of NICE guidance. Slide set. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011. 19 p. (Clinical guideline; no. 121). Electronic copies: Available from the NICE Web site .
- Lung cancer. The diagnosis and treatment of lung cancer. Baseline assessment tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011. (Clinical guideline; no. 121). Electronic copies: Available from the NICE Web site .
- The guidelines manual 2007. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Apr. Electronic copies: Available in PDF from the NICE Archive Web site .
- The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available in PDF from the NICE Archive Web site .

Patient Resources

The following is available:

- The diagnosis and treatment of lung cancer. Understanding NICE guidance - information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2011 Apr. 16 p. Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site . Also available in Welsh from the NICE Web site .

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NGC Status

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